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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/242,202	NELSON ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33,36-44 and 60-110* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33,36-44 and 60-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/16/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on October 25, 2004 have been entered. Claims 2-6, 8, 9, 11, 17, 18, 21, 22, 24-26, 32, 33, 39-43, 64-68, 70, 71, 73, 74, 78-80, 83, 84, 86-88, 94, 95, 99-104, 109, and 110 have been amended. Currently, claims 1-33, 36-44, and 60-110 are pending in the application and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 10/25/04 response would be addressed to the extent that they apply to current rejection.

Claim Objections

Claims 64 and 109 are objected to because the amended claims recite "SEQ ID No: 34 and 35" to replace "as depicted in figure 2". However, these sequence identification numbers are inconsistent with figure 2, which identified as SEQ ID No: 33 and SEQ ID No: 34. Further, SEQ ID No: 35 is an amino acid sequence, cannot be the sequence depicted in figure 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-33, 36-44, 60-110 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record and following.

In the response, Applicants first argue that the Office fails to meet its burden of showing why it would require undue experimentation to use other promoters, 3' splice sites and poly-A sequences.

In reply to this argument, the Office has cited numerous teachings in the art (see particularly pages 10-13 of the Office action mailed 2/13/02) showing that the efficiency of various regulatory elements varies from cell to cell, and from gene to gene. Thus, the expression efficiency of a construct is highly unpredictable when one assembles different promoters and other regulatory sequences for expressing a particular gene in a specific cell type, and it is highly unpredictable whether the resulted construct could be used as a vaccine composition in humans. Neither the specification nor the response provides evidence contrary to the cited teachings of record, particularly those taught by *Nettelbeck et al, Miller et al,* and *Verma*; nor they provide guidance as how to overcome the art known hurdles. To this end, the court states, "IN CHEMICAL CASE WHERE APPLICANT DISCLOSES THAT ONE SPECIES OF A CLASS OF CHEMICALS WILL ACCOMPLISH CERTAIN PURPOSE WITHOUT NAMING ANY OTHERS OF CLASS TO WHICH IT BELONGS OR WITHOUT SO DESCRIBING THE SPECIES AND ITS MODE OF OPERATION AS TO CALL ATTENTION TO FACT THAT OTHER MEMBERS OF CLASS ARE ITS EQUIVALENTS AND WILL PERFORM SAME FUNCTIONS, HE IS NOT ENTITILED TO BROADER SCOPE OF DISCLOSED INVENTION BY CLAIMING WHOLE GROUP EVEN THOUGH THOSE SKILLED IN ART MAY KNOW THAT IN SOME RESPECTS AT LEAST DIFFERENT MEMBERS OF GROUP ARE EQUIVALENTS; CERTAIN MEMBERS OF WELL-DEFINED GROUP OF CHEMICALS MAY BE EQUIVALENTS FOR ONE PURPOSE AND NOT EQUIVALENT FOR ANOTHER. (*In re Soll*, 97 F.2d623, 38 USPQ 189

CCPA 1938, emphasis added). Accordingly, the disclosure fails to provide an enabling disclosure to support the full scope of the claimed invention.

Applicants then argue that if any enabled use is disclosed by the specification or known to the skilled artisan, this rejection is improper. In response, this argument is true for the one enabling embodiment, i.e. the pITL vector with a human RANTES promoter and 3' splice and polyA from human growth hormone as indicated previously. However, for the vast majority of the humanized polynucleotide vectors encompassed by instant claims, the disclosure fails to provide even one enabled use. Accordingly, the argument is not persuasive.

Applicants go on to argue that most claims do not recite that effective immunotherapy is achieved; claim 16 does not justify the heightened standard, and it would be an error to read the same into the claims. In response, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. "WHEN A COMPOUND OR COMPOSITION CLAIM IS LIMITED BY A PARTICULAR USE, ENABLEMENT OF THAT CLAIM SHOULD BE EVALUATED BASED ON THAT USE". (MPEP 2164.01c) Since the specification clearly teach the objective to construct "a humanized vector" that lacks an antibiotic resistance is to avoid undesired anti-viral (vector) immune response, and to prevent the theoretical risk of transferring antibiotic resistance to normal host flora (e.g. Specification, page 6, lines 15-20), the utility of the vector is clearly for use in humans for genetic vaccination and gene therapy. MPEP also teaches, "DURING PATENT EXAMINATION, THE PENDING CLAIMS MUST BE 'GIVEN THEIR BROADEST REASONABLE INTERPRETATION CONSISTENT WITH THE SPECIFICATION'. *In re Hyatt*, 211 F.3d

1367, 1372, 54 USPQ2d 1664, 1667 Fed. Cir. 2000" (MPEP 2111). Hence, it is proper to evaluate the vectors according to the standard set forth in MPEP.

When responding to the cited *Moingeon et al* reference, Applicants argue that they provide a new and useful antigen-presenting platform. In reply, *Moingeon et al* was cited to evidence the under-developed state of the art, the Office acknowledged the enabled embodiment, and the rejection is based on the lack of support for the full scope of the claims.

Applicants then allege that the Office dismissed the Nelson declaration because it fails to specify the route of administration. In response, this characterization of the Office action is in error. The Office acknowledges the later submitted declaration supplemented the specification by showing a protective effect of a pITL-rNeu vector in a mouse tumor model; this is sufficient to enable the pITL-rNeu vector. The Office pointed out the declaration fails to support the full scope of the claimed method because it fails to disclose the means of administering the vector for the disclosed protective effect because claims encompass any route of administration. The Office also cited the skilled in the art to provide reasoning why the route of administration is important for an enabling disclosure (*Bodey et al, McCluskie et al*, *Torres et al,* and *Nakano et al*). These cited teachings establish that at the time of the instant filing date, the state of the art for DNA vaccination is far from routine, thus, specific not general guidance is required for the claimed invention.

With respect to *Manning* declaration, *Manning* generally stated that numerous human promoters and other regulatory elements are known in the art, choosing the

elements to construct a vector, and screening vectors for the ability to induce an immune response are matters of routine experimentation. However, this statement contradicts the cited art of record as taught by *Nettelbeck et al, Miller et al,* and *Verma*. *Manning* fails to explain why his opinion differs from the cited art of record also taught by the skilled artisans, and *Manning* does not address how to overcome the art-known hurdles as taught in the cited art of record. Applicants are reminded that the case law teaches, "IN CHEMICAL CASE WHERE APPLICANT DISCLOSES THAT ONE SPECIES OF A CLASS OF CHEMICALS WILL ACCOMPLISH CERTAIN PURPOSE WITHOUT NAMING ANY OTHERS OF CLASS TO WHICH IT BELONGS OR WITHOUT SO DESCRIBING THE SPECIES AND ITS MODE OF OPERATION AS TO CALL ATTENTION TO FACT THAT OTHER MEMBERS OF CLASS ARE ITS EQUIVALENTS AND WILL PERFORM SAME FUNCTIONS, HE IS NOT ENTITILED TO BROADER SCOPE OF DISCLOSED INVENTION BY CLAIMING WHOLE GROUP EVEN THOUGH THOSE SKILLED IN ART MAY KNOW THAT IN SOME RESPECTS AT LEAST DIFFERENT MEMBERS OF GROUP ARE EQUIVALENTS; CERTAIN MEMBERS OF WELL-DEFINED GROUP OF CHEMICALS MAY BE EQUIVALENTS FOR ONE PURPOSE AND NOT EQUIVALENT FOR ANOTHER. (*In re Soll*, 97 F.2d623, 38 USPQ 189 CCPA 1938, emphasis added). Since applicants only disclosed one species of the whole group of humanized expression vectors, they have not provide an enabling disclosure to show that the other members of the family/group are indeed the equivalent of the disclosed species either by exemplification or other descriptions, it would require undue experimentation for the skilled intending to practice the invention to figure out for themselves which member of the group has the function as a genetic vaccine of gene therapy carrier. To this end, the court has determined, "LAW REQUIRES THAT THE DISCLOSURE IN APPLICATION SHALL INFORM THOSE SKILLED IN THE ART HOW TO USE APPLICANT'S ALLEGED DISCOVERY, NOT HOW TO FIND OUT HOW TO USE IT FOR

THEMSELVES" *In re Gardner* 166 USPQ 138 (CCPA) 1970. Accordingly, for reasons of record and set forth *supra*, the rejection stands.

Applicants failed to address the issue concerning the mammalian homolog of any human promoter, thus, for reasons of record, the specification further fails to provide an enabling disclosure to support the full scope of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-33, 36-44, 60-110 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants failed to address this section of the rejection, and thus for reasons of record, the rejection stands.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-3, 7, 10, 15-19, 23-31, 36-37, 41-44, and 65 stand rejected under 35 U.S.C. 102(e) as being anticipated by *Roop et al* (US 6,143,727).

Applicants first argue that *Roop et al* simply does not teach a vector lacking vector-derived polypeptides. In reply, as indicated in pages 15-16 of the Office action mailed 2/13/02, the cassette taught in column 5, lines 55-67, and vectors illustrated in figures 4, 5, 6, 8, 10, 11 are vectors lacking vector derived polypeptides.

Applicants then argue that even if Roop et al taught such vector and vector contains no antibiotic resistance, they are irrelevant because the claims requires absence of polypeptides encoded *anywhere* by the vector. In response, the claims do not have the limitation that claimed vector is absence of polypeptides encoded anywhere by the vector, and the claims only have a limitation that a vector lacking nucleic acid sequences encoding a *vector-derived* polypeptide. Moreover, as indicated by the applicants, the vector provides a new platform for antigen presentation, thus if the vector does not encodes a polypeptide anywhere, what is the utility of the claimed vector? Apparently, this argument is inconsistent with the disclosure of the specification.

Accordingly, for reasons of record and set forth above, the rejection stands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 15-31, 36, 37, 41-44, 60-62, 65-71, 77-92, 96-107, 110 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carrano et al* (US

6,197,755), in view of *Nelson et al* (J Immunol 1993;151:2601-12, IDS), *Nelson et al* (J Immunol 1996;157:1139-48, IDS), and *Eastman et al* (US 6,103,470), and evidenced by Promega Datasheet for pGL-2, and *Eggertsson et al* (IDS).

Claims 15, 16, 23, 78, 85 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carrano et al* (US 6,197,755), *Nelson et al* (J Immunol 1993;151:2601-12), *Nelson et al* (J Immunol 1996;157:1139-48, IDS), and *Eastman et al* (US 6,103,470) as applied to claims 1-9, 15-31, 36, 37, 41-44, 60-62, 65-71, 77-92, 96-107, 110 above, and further in view of *Zurr et al* (US 5,648,235).

Claims 32, 33, 38-40, and 93-95 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carrano et al* (US 6,197,755), *Nelson et al* (J Immunol 1993;151:2601-12), *Nelson et al* (J Immunol 1996;157:1139-48, IDS), and *Eastman et al* (US 6,103,470) as applied to claims 1-9, 15-31, 36, 37, 41-44, 60-62, 65-71, 77-92, 96-107, 110 above, and further in view of further in view of *Danko et al* (Gene Ther 1994;1:114-121).

Claims 10, 11, 72, 73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carrano et al* (US 6,197,755), *Nelson et al* (J Immunol 1993;151:2601-12), *Nelson et al* (J Immunol 1996;157:1139-48, IDS), and *Eastman et al* (US 6,103,470) as applied to claims 1-9, 15-31, 36, 37, 41-44, 60-62, 65-71, 77-92, 96-107, 110 above, and further in view of further in view of *Levinson* (US 6,084,083).

Claims 12, 63, 74, 108 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Carrano et al* (US 6,197,755), *Nelson et al* (J Immunol 1993;151:2601-12), *Nelson et al* (J Immunol 1996;157:1139-48, IDS), and *Eastman et*

al (US 6,103,470) as applied to claims 1-9, 15-31, 36, 37, 41-44, 60-62, 65-71, 77-92, 96-107, 110 above, and further in view of *Theofan et al* (US 5,674,834), and *Sloma et al* (US 5,891,701).

The above rejections would be addressed together as follows since applicants argued them together.

Applicants first argue that Carrano does not teach a vector lacking vector derived polypeptide, and Eastman fails to cure that failing of Carrano.

In response, as indicated in the previous Office action, *Carrano et al* teach a polynucleotide vector, lacking vector derived polypeptide-coding sequence such as shown in fig. 1. Again, applicants wrongly characterized the Office action concerning the teaching of *Eastman et al,* which was cited to supplement the teachings of *Carrano et al* and *Nelson et al* for lacking an antibiotic resistance.

Applicants then argue neither Carrano nor Eastman teaches a sequence acceptance site having an interrupted palindrome recognition sequence. In response, it is noted that the features upon which applicant relies (i.e., a sequence acceptance site having an interrupted palindrome recognition sequence) are not recited in the rejected claim(s). The claims only requires a sequence acceptance site, which has been taught by Nelson et al. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Further, it is noted that applicants attack each reference separately, and ignore the fact that the rejection relies on the combined references. In response to applicant's

arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants also argue it is improper not given patentable weight for the use of an interrupted palindrome recognition sequence. In response, the phrase "cDNA derived from rtPCR cloning via unique sites within an interrupted palindrome recognition sequence for a restriction endonucleases" defines the cDNA that may be inserted in the sequence acceptance site. This recitation defines the cDNA not by its structure, but by how it is produced, i.e. "derived from rtPCR cloning via unique sites within an interrupted palindrome recognition sequence for a restriction endonucleases". For purpose of prior art exclusion, there is no limitation on the structure of the cDNA, and thus the cDNA encompasses any cDNA, because no matter how the cDNA was generated (derived), as long as the end product is the same, it meets claim limitation. This is why the product-by-process case law (*In re Thorpe*, 227 USPQ 964 Fed. Cir. 1985) applies.

Accordingly, for reasons of record and set forth *supra*, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vector and methods taught by *Carrano et al* by choosing the RANTES promoter as the preferred promoter as taught by *Nelson et al* and replacing the antibiotic resistance gene with a suppressor tRNA or a small element as taught by *Eastman et al* with a reasonable expectation of success. Given the detailed knowledge of RANTES promoter

in immune regulation as taught by *Nelson et al*, the ordinary skilled artisan would have been motivated to modify the claimed invention when regulating immune system are the subject of interest; and given the knowledge in the art concerning the disadvantage of antibiotic selection marker and solution to it as taught by *Eastman et al*, the ordinary skilled artisan would have been motivated to modify a therapeutic vector intended for human use because using non-antibiotic selectable marker could avoid the potential problem of antibiotic resistance in humans. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 38-40, stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Roop et al* (US 6,143,727) and in view of *Danko et al* (Gene Ther 1994;1:114-121), for reasons of record and arguments have been addressed above under 35 USC 102 rejection.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Ram R. Shukla** can be reached on 571-272-0735. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. JANICE LI, M.D.
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March 1, 2005